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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,455	07/08/2002	Mordechai Erez	02/23383	3348
7590 03/03/2004			EXAMINER	
G E Ehrlich 1995 Anthony Castorina Suite 207 2001 Jefferson Davis Highway Arlington, VA 22202			MCKENZIE, THOMAS C	
			ART UNIT	PAPER NUMBER
			1624	
DATE MAILED: 03/03/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/069,455

**Applicant(s)**

EREZ ET AL.

**Examiner**

Thomas McKenzie Ph.D.

**Art Unit**

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1,2 and 6-40 is/are rejected.
- 7) ☒ Claim(s) 3-5 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 104.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1203. 6) ☐ Other:

**DETAILED ACTION**

1. This action is in response to an application filed on 7/8/02. There are forty claims pending and forty under consideration. Claims 1-5 are compound claims. Claims 6-13 are composition claims. Claims 14-40 are use claims. This is the first action on the merits. The application concerns some iminodibenzyl compounds, compositions, and uses thereof.

***Oath/Declaration***

2. The present Application is in scanned form. The Examiner can see the notice sent to Applicants concerning the missing declaration, Applicants' letter concerning the response, and the notice that the oath has been received. However, the Examiner cannot see the actual oath in the electronic file. To be safe perhaps another copy of the signed declaration should be added to the file.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6, 14, 16, 21-23, and 30-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 1, 6, 14, 21, 23, 30, 32, and 34 Applicants offer "diamino" as a possible R<sup>1</sup>. What is the structure of "diamino"? It is not defined in the specification. An amino group is –

NH<sub>2</sub>. Is "diamino" H<sub>2</sub>N-NH<sub>2</sub>? Or could it be -NH-NH<sub>2</sub>? Could the two amino groups be attached to a third trivalent atom like phosphorus, -P(NH<sub>2</sub>)<sub>2</sub>? Could the two amino groups be attached to a linking alkylene chain, H<sub>2</sub>N-(CH<sub>2</sub>)<sub>n</sub> NH<sub>2</sub>? Could it be an aminoalkylene chain with a second amino substituent, -(CH<sub>2</sub>)<sub>n</sub>-CH(H<sub>2</sub>N)-(CH<sub>2</sub>)<sub>n</sub>-NH<sub>2</sub>? What ever choice Applicants make must be supported in the specification.

4. Claims 6, 14, 23, 32, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In each of these claims, in the seventh line under the figure, Applicants have the limitation, "wherein n is an integer". Are there any size limits upon n, is it restricted to 0 to 5 or could it be infinitely large?

5. Claim 18 recites the limitation "wherein A is \*\*\* or C=O" in line 1. There is no antecedent basis for this limitation in the parent claim 14, which restricts A to CH or CR<sub>2</sub>R<sub>3</sub>. The Examiner suggests deleting this limitation from claim 18.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing these diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the iminodibenzyl compounds such as present here. In addition, it is presumed that “prevention” of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of cardiac arrhythmias and other cardiac diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners

in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent cardiac arrhythmias generally. That is, the skill is so low that no compound effective generally against such cardiac disorders has ever been found let alone one that can prevent such conditions.

The Examiner suggests deletion of the word “preventing”.

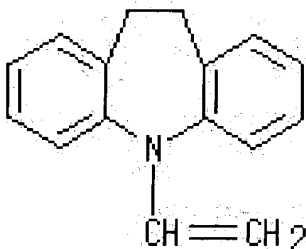
***Claim Rejections - 35 USC § 102***

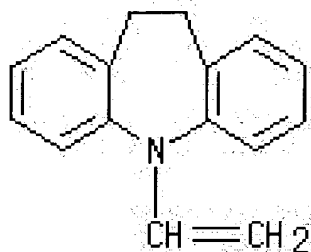
7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

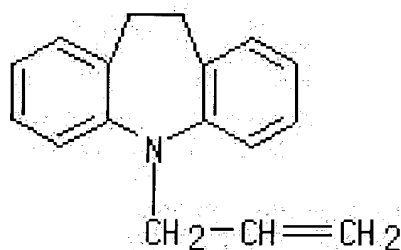
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lin (Journal of Polymer Science, Polymer Chemistry Edition). The compound shown below fits formula (II) with  $R_Q = R_T = \text{hydrogen}$ ,  $q = t = 1$ , and  $R^1 = \text{the unsaturated alkyl group vinyl}$ . It has Registry Number 73046-29-4 and is found in \*\*\* of the reference.



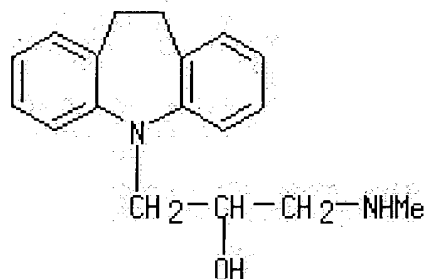


8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Gozlan (Journal of Heterocyclic Chemistry). The compound shown below fits formula (II) with  $R_Q = R_T = \text{hydrogen}$ ,  $q = t = 1$ , and  $R^1 = \text{the unsaturated alkyl group allyl}$ . It has Registry Number 74074-21-8 and is found in Experiments 6-9, page 1570 of the reference. The product of these experiments is not named explicitly in the reference but discussion of N-alkylation of 1 in the first paragraph of page 1569, combined with the structure of the alkylating agent make clear that the compound pictured below must be the product obtained.

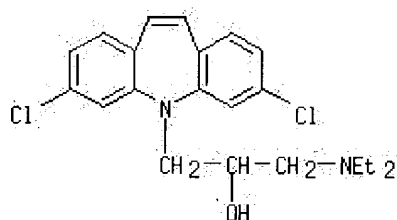


9. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Buckler ('281). The compound shown below fits formula (II) with  $R^1 = R_Q = R_T = \text{hydrogen}$ ,  $q = t = 1$ , and  $R^1 = \text{the amino alcohol group with } n = 1$ , and  $R'' = \text{methyl}$ . It has Registry Number 91325-19-8 and is found in Fig. 2 of the reference. It is

called compound (5) and reference to its method of synthesis is found in lines 64-65, column 11.



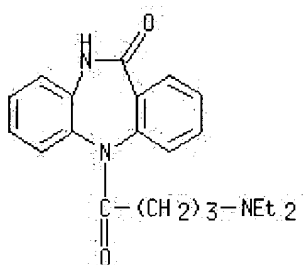
10. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Schindler ('281). The compound shown below fits formula (II) with  $R_Q = R_T = \text{chlorine}$ ,  $q = t = 1$ , and  $R^1 = \text{the amino alcohol group } \alpha\text{-(diethylaminomethyl)-ethanol}$ , with  $n = 1$ , and  $R' = R'' = \text{ethyl}$ . It has Registry Number 102374-72-1 and is found in claim 2 of the reference.



11. Claims 23, 30, 32, 34, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ruger ('432, cited by Applicants). The compound shown below fits the formula of claim 14 with  $A = \text{C=O}$ ,  $B = \text{NH}$ ,  $R_Q = R_T = \text{hydrogen}$ ,  $q = t = 1$ , and  $R^1 = \text{C(=O)(CH}_2\text{)}_n\text{NR'R''}$ , with  $n = 3$ , and  $R' = R'' = \text{ethyl}$ . It has Registry Number



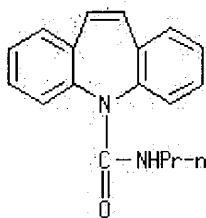
134000-64-9 and is found in Example 2, columns 9 and 10 of the reference. The passage spanning lines 18-31, column 2 teaches that this compounds is effective for the treatment of arrhythmias, tachyarrhythmia, and bradyarrhythmia. Line 1, page 6 teaches pharmaceutical solutions and lines 45-51, page 6 describe intravenous administration of other compounds of this invention. Thus, the concept of parenteral administration of the above compound is present in Ruger ('432, cited by Applicants). Applicants' claims 23 and 34 are drawn to treating cardiac fibrillation, Applicants claim 32 is drawn to treating cardiac ischemia. Cardiac fibrillation is an extreme form of arrhythmia and of tachacardia. In the alternative it would be obvious to use a compound known to active against heart arrhythmias and rapid heart beat to treat other cardiac diseases.



***Allowable Subject Matter***

12. Claims 3-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 14, 15, 21, 23, 24, 30, 32, 34, and 35 are allowable over Kawashima ('091). The compound

shown below fits the formula of claim 14 with  $A = B = \text{CH}$ ,  $R' = R_Q = R_T =$  hydrogen,  $q = t = 1$ , and  $R^1 = \text{C}(=\text{O})(\text{CH}_2)_n\text{NR}'\text{R}''$ , with  $n = 0$ , and  $\text{R}'' = \text{propyl}$ . It has Registry Number 41359-00-6 and is found in Example 1, lines 3-18, column 4 of the reference. However, this is only an intermediate and no biological activity for this substance is reported.



### ***Conclusion***

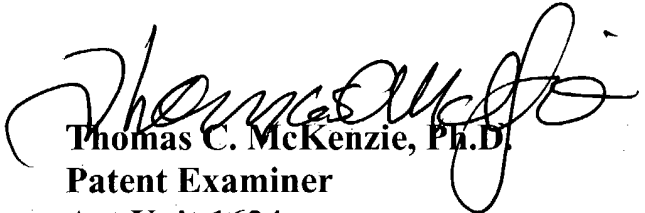
13. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

14. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose

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telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, Acting-SPE of 1624 at (571)-272-0661.

  
**Thomas C. McKenzie, Ph.D.**  
**Patent Examiner**  
**Art Unit 1624**

TCMcK